REMARKS

In response to the Office Action of September 17, 2003, Applicants have amended the claims, which when considered with the following remarks, is deemed to place the present application in condition for allowance. By this amendment, claims 32, 67, 70, 71, 85, and claims 96-99 have been canceled without prejudice. Favorable consideration of all pending claims is respectfully requested. Cancellation or amendment of claims should not be interpreted as acquiescence to the Examiner's rejections but rather as Applicants' advancing prosecution of this application. Applicants reserve the right to prosecute in this or another application the subject matter of one or more cancelled claims or one or more claims prior to this amendment.

In the first instance, Applicants through the undersigned, thank Examiner Rao for helpful suggestions provided during the telephone interview of December 16, 2003.

In the Office Action of December 9, 2002, claims 29 and 61 have been rejected under 35 U.S.C.§ 112, second paragraph, as allegedly indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Specifically, the metes and bounds of the phrase "amino acids corresponding to α-N-acetylglucosaminidase" is not clear to the Examiner. As presently amended, claims 29 and 61 recite "an amino acid sequence as set forth in SEQ ID NO:2." Withdrawal of the rejection of claims 29 and 61 is therefore warranted.

Claims 97 and 98 depending therefrom, have been rejected under 35 U.S.C.§ 112, second paragraph, as allegedly indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 97 and 98 are cancelled by this amendment, rendering the rejection moot.

Claims 19-36, 60-67, 70-71, 85, and 96-99 have been rejected under 35 U.S.C. §112, first paragraph, as allegedly directed to non-enabled subject matter. On page 3 of the Office Action, the Examiner has indicated that the specification is enabling for a recombinant enzyme having α-N-acetylglucosaminidase activity and an amino acid sequence as set forth in SEQ ID NO:2 or an amino acid sequence that is 80% identical to SEQ ID NO:2 or an amino acid sequence that is encoded by a polynucleotide capable of hybridizing to SEQ ID NO:1 or SEQ ID NO:3 under high stringency conditions, but is allegedly non-enabling for other embodiments of the present invention as claimed by Applicants. In response to the rejection and in order to advance prosecution of this application, independent claims 19, 35, and 60 have been amended to recite that the recombinant α-N-acetylglucosaminidase "comprises at least one of an amino acid sequence as set forth in SEQ ID NO:2, an amino acid sequence having at least 80% sequence identity to the amino acid sequence set forth in SEQ ID NO:2, or an amino acid sequence encoded by a polynucleotide capable of hybridizing to SEQ ID NO:1 or SEQ ID NO:3 under high stringency conditions." Claims 67-71, 85, and 96-99 have been cancelled. The remaining rejected claims depend from presently amended clams 19, 35, or 60. Withdrawal of the rejection of claims 19-36, 60-68, 70-71, 85, and 96-99 under the enablement provision of 35 U.S.C. §112, first paragraph, is therefore respectfully requested.

Claims 19-31, 35, 36, 60-66, 70-71, and 96-98 have been rejected under 35 U.S.C. §112, first paragraph, as allegedly violative of the written description requirement. It is the Examiner's position that the rejected claims recite the enzyme based on function without any description of the structure. In order to advance prosecution of this application, independent claims 19, 35, and 60 are presently amended to recite that the recombinant α-N-acetylglucosaminidase "comprises at least one of an amino acid sequence as set forth in SEQ ID NO:2, an amino acid

sequence comprising at least 80% sequence identity to the amino acid sequence set forth in SEQ ID NO:2, or an amino acid sequence encoded by a polynucleotide capable of hybridizing to SEQ ID NO:1 or SEQ ID NO:3 under high stringency conditions." The remaining rejected claims depend from presently amended claims 19, 35, or 60. Withdrawal of the rejection of claims 19-36, 60-68, 70-71, 85, and 96-99 under the written description requirement of 35 U.S.C. §112, first paragraph, is therefore respectfully requested.

Applicants acknowledge withdrawal of the previous rejection of claims 19-20, 26-29, 32-36, 85, 96, and 99 under 35 U.S.C.§102(b) as allegedly anticipated by Zhao et al. (1994) *American Journal of Genetics*, Vol. 55:A252, Abstract 14 73.

Claims 19-20, 26-29, 32-36, 85, 96, and 99 have been rejected under 35 U.S.C. §102(b) as allegedly anticipated by Zhao et al. (1995) "The gene encoding α-N-acetylglucosaminidase and mutations underlying Sanfilippo B syndrome" *American Journal of Human Genetics 5*: abstract 1059 A185 (hereinafter "Zhao et al. 1995"). These same claims were rejected in the previous office action of December 9, 2002, under 35 U.S.C.§ 102(a). In the office action of September 17, 2003, page 11, the Examiner has indicated that the previous rejection of these claims under 35 U.S.C. §102(a) was inadvertent and should have been under §102(b).

Applicants respectfully submit that the present application is a divisional application of U.S. Serial No. 09/077,354, now U.S. Patent No. 6,255,096. U.S. Serial No. 09/077,354 was filed as a nation phase (section 371) application corresponding to PCT/AU96/00747. PCT/AU96/00747 was filed on November 22, 1996, designating the U.S. among other countries. PCT/AU96/00747 was based on Australian provisional application PN 6748, filed November 23, 1995. Zhao et al.(1995) was published sometime in 1995. 35 U.S.C.§ 365(c) provides that an international application designating the United States shall be entitled to the right of priority

based on a prior foreign application or a prior international application designating at least one country other than the United States. 35 U.S.C. § 121 provides that a divisional application complying with the requirements of 35 U.S.C. § 120 shall be entitled to the benefit of the filing date of the original application. Section 120 provides that an application filed by an inventor or inventors named in a previously filed application shall have the same effect, as to the invention, as though filed on the date of the prior application, if filed before the patenting or abandonment or termination of proceeding s of the prior application. Thus, the present application, which was filed before issuance of U.S. Patent No. 6,255,096, has an effective filing date of November 23, 1995. Since Zhao et al. (1995) was published sometime in 1995, which date is *not* more than one year prior to the effective filing date of the present application, Zhao et al. (1995) is not a proper reference under 35 U.S.C. 102(b). Withdrawal of the rejection of claims 19-20, 26-29, 32-36, 85, 96, and 99 under 35 U.S.C. §102(b) is therefore respectfully requested.

Claims 21-25, 30-31, 60-67, 70-71, and 97-98 have been rejected under 35 U.S.C. §103(a) as allegedly unpatentable over Zhao et al. (1995) *American Journal of Genetics*, Vol. 57:A185, Abstract 1059, ("Zhao et al. 1995"). In response to the rejection, Applicants respectfully submit that it could not have been obvious to "take the recombinant enzyme taught by Zhao et al. (1995) and make it in a pharmaceutical composition to treat MPS IIIB disorder" as stated by the Examiner on page 14 of the office action, since Zhao et al. (1995) do not teach a recombinant enzyme. As submitted by Applicants previously, the teaching of Zhao et al. (1995) is limited to a reporting of the cloning of the human gene and cDNA encoding α-N-acetylglucosaminidase. There is no indication in Zhao et al. (1995) that the gene or cDNA was ever expressed in a recombinant vector to produce a recombinant α-N-acetylglucosaminidase. No nucleotide sequence for either the cDNA or the gene is provided. Thus, one skilled in the art

having Zhao et al. (1995) in hand could not have been able to make a recombinant α-N-acetylglucosaminidase as presently claimed. The authors' own uncertainty in Zhao et al. (1995) concerning 93 nucleotides of the cDNA with respect to whether such nucleotides were intronic, coupled with a total non-disclosure of *any* nucleotide sequence for an α-N-acetylglucosaminidase further indicate a lack of reasonable expectation of success found in the prior art.

On page 15 of the office action, the Examiner has stated that "there was no need for the Examiner to resort to hind-sight reconstruction in view of Zhao et al. PNAS USA, June 1996, Vol. 93:6101-6105 reference (and the enclosed Swissprot (accession no. P54802) amino acid sequence alignment) which discloses the amino acid sequence of the recombinant NAG which is 100% identical to SEQ ID NO:2 (see first para, column 2 on page 6101 of Zhao(a) et al. wherein a reference is made to Zhao(b) et al.)."

In response to this statement, Applicants respectfully submit the following. Zhao et al. PNAS USA, June 1996, Vol. 93:6101-6105, was published *after* the effective filing date of the present application. The *deduced* amino acid sequence for human α-N-acetylglucosaminidase is shown in Figure 2 of this reference. Applicants respectfully submit that any teaching provided by Zhao et al. PNAS (1996) and related to α-N-acetylglucosaminidase is limited to enzyme purification and activity assays *which were performed on enzyme isolated from bovine testes. See* page 6101, column 2. Moreover, even the deduced amino acid sequence provided by Zhao et al. PNAS (1996) was not available to skilled artisans as of the effective filing date of the present application. In addition, the Swissprot (accession no. P54802) is indicated as having been created on October 1, 1996, which date is also after the effective filing date of the present application.

Since Zhao et al. (1995) provides no nucleotide or amino acid sequence information, nor indicate that any recombinant α-N-acetylglucosaminidase was ever produced, the claims as presently amended could not have been obvious as of the effective filing date of the present application. Withdrawal of the rejection of claims 21-25, 30-31, 60-67, 70-71, and 97-98 under 35 U.S.C. §103(a) is therefore respectfully requested.

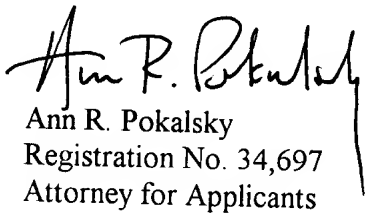
Claims 19-32, 35-36, 60-67, 70-71, 85, and 96-99 have been rejected under 35 U.S.C. 103(a) as allegedly unpatentable over Sasaki et al. (1991) *J. Biochem. 110*(5):842-846 and the common knowledge of cloning in the art of molecular biology. Sasaki et al. has been cited for teaching purification of a human α-N-acetylglucosaminidase (NAG) from human liver. The reference has also been cited for teaching that the enzyme is 80 kDa when tested by SDS/PAGE and that a deficiency of the enzyme is known to cause MPS IIIB or Sanfilippo B syndrome, a severe neurodegenerative disease in humans. The reference does not teach the recombinant form of the enzyme or a pharmaceutical composition comprising the enzyme or use of the same in treating MPS IIIB or Sanfilippo B syndrome. Applicants further submit that the reference teaches neither a nucleotide sequence nor a corresponding amino acid sequence for human α-N-acetylglucosaminidase (NAG).

As presently amended, claims 19-31, 35-36, and 60-66 recite a recombinant α-N-acetylglucosaminidase that "comprises at least one of an amino acid sequence as set forth in SEQ ID NO:2, an amino acid sequence comprising at least 80% sequence identity to the amino acid sequence set forth in SEQ ID NO:2, an amino acid sequence encoded by a polynucleotide capable of hybridizing to SEQ ID NO:1 or SEQ ID NO:3 under high stringency conditions. There is no suggestion in Sasaki et al. for the present invention as recited in claims 19-31, 35-36, and 60-66. Absent a suggestion in the combination of teachings provided by Sasaki et al. and the

common knowledge of cloning in the art of molecular biology, for a recombinant α-N-acetylglucosaminidase that comprises at least one of an amino acid sequence as set forth in SEQ ID NO:2, an amino acid sequence comprising at least 80% sequence identity to the amino acid sequence set forth in SEQ ID NO:2, or an amino acid sequence encoded by a polynucleotide capable of hybridizing to SEQ ID NO:1 or SEQ ID NO:3 under high stringency conditions, the present invention is not obvious. Withdrawal of the rejection of claims 19-32, 35-36, 60-67, 70-71, 85, and 96-99 under 35 U.S.C.§ 103(a) is therefore warranted.

In view of the foregoing remarks and amended claims, it is firmly believed that the present application is in condition for allowance, which action is earnestly solicited.

Respectfully submitted,



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